M57-1
III
GENERAL
To Subcommittee III on.

267

August 30, 1972

Elliott Middleton, Jr., M.D.
Director, Clinical Services
and Research
Children's Asthma Research Institute
and Hospital
3401 West 19th Avenue
Denver, Colorado 80204

Dear Dr. Middleton:

We are pleased to inform you that the National Institutes of Health, acting for the entire Department of Health, Education, and Welfare, has reviewed and accepted the general assurance dated March 14, 1972, as subsequently amended, submitted by the Children's Asthma Research Institute and Hospital, as being in essential compliance with the requirements contained in DHEW Grants Administration Manual Chapter 1-40 effective April 15, 1971.

It is necessary that this office be kept informed on a current basis of any changes in policies, procedures, or committee composition relating to this requirement.

We appreciate your cooperation in this matter. We welcome any comments or suggestions you may wish to make with regard to the administration of this policy.

Sincerely yours,

Stephen P. Hatchett, Ph.D.
Director, Division of Research Grants

children's asthma research institute & hospital
3401 west 19th avenue / denver, colorado 80204 / 433-2591
Elliott Middleton, Jr., M.D.,
Director, Clinical Services and Research

August 9, 1972

R. C. Backus, Ph. D.
Institutional Relations Branch
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20014

Dear Dr. Backus:

Thank you for your letter of July 24 and your thoughts about CARIH's Part Two section of the institutional general assurance.

I have essentially eliminated the word "research" from the assurance and employed the more general term "project" by and large. In some places the word has simply been dropped.

With regard to the relationship of the Parents' Application form to the assurance, I hope that an addition to the second paragraph under C-a will make the situation clear.

I look forward to hearing from you soon.

Sincerely yours,

Elliott Middleton, Jr., M. D.

EM:emb
Enclosure
P.S.: Copies of biographic sketches of members of the Ethics Committee were sent to you previously with the original statement.

em

Implementing guidelines, Part Two of a General Institutional Assurance

A. Statement of Principles

a. Any activity which includes a human being as a subject must provide for the individual's safety, health and welfare. Specifically, this includes any individual who may be at risk as a consequence of participation as a subject in research, development, demonstration or any other activities directly supported by Department of Health, Education and Welfare (DHEW) funds, whether provided through research, training or other types of grants, awards or contracts or financed by any other source.

Regardless of the source of support, all projects involving human subjects are periodically reviewed as described below. (Section B)

b. Subjects may include persons involved in behavior science studies; normal volunteers; donors of specific services; inpatients and outpatients; unborn, living or dead donors of body fluids, organs and tissues; and members of the general population who may be involved in any aspect of the project.

c. The Code of Ethics on Human Experimentation at CARIH is directly and completely drawn from the Declaration of Helsinki, 1964, a copy of which is appended to all copies of this assurance distributed to members of the Ethics Committee and the professional staff.

d. A subject is accepted in a project only after he or his legally authorized guardian or next of kin has consented to his participation. Such consent is considered valid only if the following six basic elements are provided:

1. A fair explanation of the procedures to be followed, including an identification of those which are experimental;

2. A description of the attendant discomforts and risks;

3. A description of the benefits to be expected;

4. A disclosure of appropriate alternative procedures that would be advantageous for the subject;

5. An offer to answer any inquiries concerning the procedures;

6. An instruction that the subject is free to withdraw his consent and to discontinue participation in the project or activity at any time.

Furthermore, the consent agreement entered into by the subject shall include no exculpatory language through which the subject would be made to waive or to appear to waive any of his legal rights or to release the institution or its agents from liability or negligence. Also, any modification or omission of these six basic requirements must have Ethics Committee justification and must be documented. Documentation requirements for informed consent will follow one of the following three forms:

1. A written consent document stating all of the basic elements of informed consent, to be signed by the subject or his authorized representative.

2. A short form written consent document indicating that the basic elements of informed consent have been presented orally to the subject. A written summary of what will be described to the patient is to receive prior approval by the Ethics Committee. This short form is to be signed by the subject or his authorized representative, and an auditor-witness to the oral presentation and to the subject's or his authorized representative's signature. A copy of the approved summary is to be signed by the persons obtaining the consent on behalf of the institution and by the auditor-witness.

3. Modification of either of the above two procedures. Any modification requires Ethics Committee approval and must be recorded in the Minutes of the Ethics Committee and signed by its Chairman.

Samples of all forms, copies of approved summaries and other relevant records will be retained.

e. We recognize that the subject does not abdicate his rights by consent to participation in a project directly supported by DHEW funds. He may withdraw his consent at any time. Further, he has the right to be secure in his person, to receive proper professional care, to enjoy privacy and confidentiality in the use of information about himself and to be free from undue embarrassment, discomfort and harassment.

B. Initial and continuing reviews. Ethics Committee Composition and Function.

a. There exists at CARIH an Ethics Committee, a standing committee of the Medical Staff. The responsibility of this committee is to evaluate projects involving human subjects. Current membership of the Committee is given on page 4.

b. Attached is a copy of the form utilized by our Ethics Committee in evaluating any project involving human subjects. Letters of parental consent are also obtained if required in the pursuit of certain projects. Samples of several letters of consent are enclosed. On the occasion of instituting a new project involving human subjects, a new and appropriate letter of parental consent is prepared for parental approval and signature.

c. The Ethics Committee meets at least monthly. Initial review of proposed projects are undertaken by this committee and continuing reviews of ongoing projects are also accomplished. In this way, we adequately protect the rights and welfare of subjects participating in projects and determine that the potential value of the study out-weighs the risk to subjects. Also, the committee determines when informed consent of subjects' parents or legal guardians will be obtained.

The committee is responsible to provide advice and counsel to project and program directors with regard to any committee actions which may influence the course of a given project and also the committee is available at any time for discussion of problems or proposed procedural changes in any ongoing project.

Monthly or more frequent meetings of the committee permits each member to be well informed about the results and problems of ongoing projects and, in turn, to implement its recommendations to project and program directors. These transactions occur formally at the time of the monthly meeting and informally from time to time in the course of daily CARIH work.

The quorum for the Ethics Committee is four members. The quorum list includes two members who are licensed to administer drugs and one who is not so licensed.

C. Special Considerations

a. CARIH is a unique patient-care setting in that patients, generally between the ages of six to sixteen, come for extended periods (up to 12 to 24 months), reside in cottages under the daily care of houseparents and attend the local public schools. In this sense, the children are in a "home away from home." A 28 bed hospital facility, with four intensive care beds, is available for general medical and emergency treatment.

Under these circumstances, CARIH is directed, authorized and empowered to give and and order for any child such surgical, medical and dental treatments and such care and guidance to the child as it may deem necessary or proper and is further empowered to act "in loco parentis" to a child at all times while he is resident at the institution. Prior to admission, the parents are required to complete and sign the "Parents' Application Form" which explicitly states these and other necessary conditions. A copy of the Parents' Application Form is attached. For the purposes of this assurance it should be clearly understood that the completed and signed Parents' Application Form applies only to medical, surgical and dental care relating to a child's general health while in residence at CARIH and does not relieve CARIH of its assurance responsibilities when a subject participates in a project directly supported by DHEW funds.

b. From time to time, normal subjects are required in the course of certain investigations. These subjects may be drawn from the general community and also occasionally are children of members of the CARIH staff. All of the commitments of the institution as described in this assurance apply to all normal subjects and the Ethics Committee is made aware of the involvement of such subjects in any project.

Current members of the Ethics Committee of CARIH:

Elliott Middleton, Jr., M. D., Director, Clinical Services and Research
Hyman Chai, M. D., Head, Division of Hospital Services
Richard W. Newcomb, M. D., Head, Immunology Division
Thomas Creer, Ph. D., Head, Behavior Science Division
Susan Rohrs, R. N., Head Nursing Division
Ray Stanley, Head, Group Living Division
Jack Gershtenson, Administrator

Biographic sketches of each of these individuals are attached.

EM:emb

CLINICAL RESEARCH AND INVESTIGATION INVOLVING HUMAN BEINGS

(Please prepare nine copies and forward to Dr. Middleton's office. Please be sure all copies are legible and use additional sheets if necessary)

TO: Ethics and Human Research Committee

FROM: _____
Principal Investigator Department

TITLE OF PROJECT: _____

1. Brief description of project as it relates to human beings. Include the question to be asked by the investigator and the methods to be used in answering this question in sufficient detail for the Committee to assess the potential hazards of the contemplated techniques.

2. Your assessment of risks and potential medical benefits of the investigation.

3. Are investigational drugs to be used? Yes___ No___(If yes, list generic name of the drug_____).

4. Will informed consent be obtained? Yes___ No___ (If yes, attach copy of correct form to be used).

5. If research is supported by grant funds, please give grant number._____

_____ _____
Approved by the Committee Date Signature of Principal Investigator Date

Samples of letters of consent

---, 3, 1971

We are writing to request your permission to ask Robert's cooperation in a study we are planning.

As you know, asthma is a condition that involves the body's immunity mechanisms. Abnormal amounts of certain kinds of substances (antibodies) are often produced that help with resistance and that are also responsible for allergic reactions. Moreover, asthma is frequently treated with steroid medicines like cortisone and prednisone. Therefore, it is important to know how these medicines can influence the body's production of antibodies.

To investigate this, we hope to immunize a number of children, some of whom are receiving steroids for their asthma and others of whom do not require such treatment. (In no case will we use steroids on anyone who does not need them, or withhold them from anyone who does need them). The substance we will use is a purified protein called KLH, derived from an animal with which no one is ever liable to come in contact in the normal course of events. This is an inedible Pacific shellfish called the keyhole limpet. The purified material has been tested and been found to be sterile and to produce no ill effects when injected into laboratory animals. We have also given injections of it to each other and have experienced no illness or discomfort except for a slight soreness at the injection site (but less than after flu shots or other similar injections). Several other investigators across the nation have also used this material in large numbers of humans and have found no adverse reactions, when it was properly used.

There are, of course, some risks that are involved with any injections, such as infections, bruises, fainting spells and the like, but all precautions will be taken to minimize these risks. Moreover, there is the possibility that a new allergy will develop to the injected material. We will, of course, test for allergies to the KLH before and after injections. The chances of ever again coming into contact with KLH seem rather small; the most realistic danger would seem to be that some doctor somewhere in the future would use the same material to test Robert's immune responses. One would expect that he would test for allergy before injecting the KLH, as we shall do.

The possibility that keyhole limpets will some day be used as food for humans is rather unlikely and very unappealing. Related animals like oysters, clams and abal-

are, of course, common foods, but no allergic reactions to these are known as a result of immunization with KLH. It is encouraging in this regard that pure KLH is rapidly destroyed in the stomach.

Therefore, we think the risks involved are minimal. We cannot think of any other possible adverse reactions, although all the results of research cannot be predicted (otherwise there would be no reason for doing it). Nevertheless, it is important to emphasize that your child will benefit by being in this study only by the added knowledge that the information gives. It will not directly help him.

Specifically, we ask your permission to request Robert's cooperation in the following: the drawing of 3 or 4 small specimens of blood; administration of KLH by injection 2 or 3 times; and skin tests before each injection (to assure the absence of allergy to KLH) and skin tests thereafter to look for the possible development of later allergy. We will offer no substantial rewards for cooperation and will, of course, use no coercion. If you or Robert decide at any time to withdraw your cooperation, you are free to do so for any reason.

If you do decide to allow us to proceed, would you please sign this letter below in the space provided and return it to us, keeping one copy for yourself? If you have any questions, please do not hesitate to write or telephone us at any time.

Sincerely,

RMJ/HT/va

I hereby consent to the performance of the procedures described above upon Robert.

Father date

Mother date

National Asthma Research Institute & Hospital
3401 west 19th avenue / denver, colorado 80204 / 433-2500
Constantine J. Falliers, M.D., Medical Director
Jack Gershtenson, Administrator
Jonas Hiken, National Director of Development

We have been studying a new drug called disodium cromoglycate or "Intal" in the treatment of asthma for the past 11 months and plan to extend our research to establish the way the drug works.

As you may be aware, part of our diagnostic work-up in understanding your child's asthma has been inhalational challenge tests to various allergens and these tests are often repeated once or several times either to confirm the results of a previous test or to study the effects of treatment.

In our further study, we plan to administer Intal to children who have known positive reactions to inhalation provocation tests 20 minutes before repeating the provocation tests and in this way to establish whether Intal does block this type of reaction.

Intal has been in use for treatment in England and Europe for over three years and has been approved for clinical trials in this country by the Federal Drug Administration and the only side effect which either we have seen or that has been reported by other investigators working with the drug has been a mild transient irritation due to inhaling the medicine. However, this drug is still an experimental drug in this country and all possible side effects may not be known.

The hazards of inhalational challenges are the risk of producing a severe attack of asthma or a more prolonged attack of asthma and are watched for particularly when we do the same inhalational challenge tests for diagnostic purposes. These risks are greatly reduced during repeated challenges because the dose which will produce a reaction is known. However, the patient will have the inconvenience of being subjected to 3 or 4 more challenge tests than he would normally have. The normal routine of keeping the child in the hospital overnight for observation after the tests will be followed.

Similar studies have been done in England and Europe and the drug has been shown to be effective in blocking reactions to inhalational provocation tests in many instances. If our results confirm these findings this may serve to be a good screening test to establish which children will benefit from the use of Intal.

We would like to include your child Robert as a subject in the study and if you agree we will also ask Robert if he will participate. Either you or Robert may withdraw from the study at any time.

If you would like to discuss this study further with us, feel free to write or call us and also discuss this with your doctor if you wish.

This study has received the approval of our Ethics Committee.

If you have no further questions, please sign below and return this letter promptly so that your child can be included in the study. The copy of the letter is for your file. Naturally, reports of the study will be included in our final medical report on your child.

Sincerely yours,

Leizer Nolk, M.D.
Assistant Head,
Division of Hospital Services

LN:sh

We understand the nature of the study outlined above and the risks involved and we agree that our child may participate in the proposed study.

3401 west 19th avenue / denver, colorado 80204 / 433-25
Elliott Middleton, Jr., M.D.,
Director, Clinical Services and Research

(1R) May I first thank you for the cooperation you have afforded Dr. Molk and myself in taking the trouble to control Joseph since his return home, especially in regard to the disodium cromoglycate (INTAL) open study.

I would like to indicate that two changes have been made in the protocol in regard to the safety aspects of INTAL by the Federal Drug Administration and I would be grateful if you would arrange for these investigations to be carried out. The results should be forwarded to me at CARIH when they have been performed, as they form part of the investigational record which must by law be kept at CARIH. They are as follows:

1. X-ray of the Chest (PA and lateral). This needs to be done only once a year.

2. CBC with RBC or Hb, BUN, blood sugar, alkaline phosphatase, SGOT, SGPT, and a routine urinalysis. These should be repeated at quarterly intervals.

If you would be good enough to forward the accounts for these measures to CARIH, they will be transferred to Fison's who will make the necessary payments.

Also, it is most important that we receive a blue "Clinical Examination and (24) History" form for each visit your patient has made. If you have not returned all of these to us, we urge you to do so immediately.

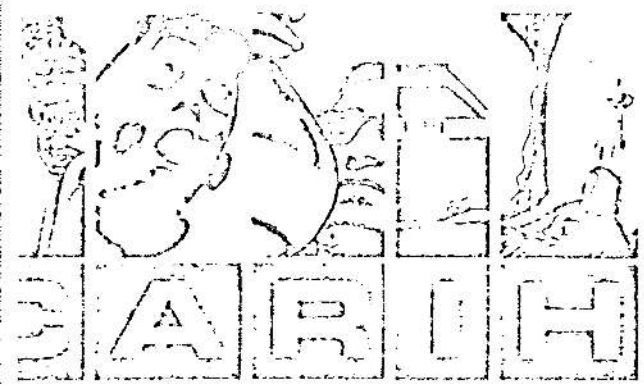
(3-12 27) Thank you again for your interest and cooperation.

Sincerely yours,

H. Chai, M.D.
Head, Division of Hospital Services

HC:sh

Intal Consent
Letter



children's asthma research institute & hospital
3401 west 19th avenue / denver, colorado 80204 / 433-2
Constantine J. Falliers, M.D., Medical Director
Jack Gerstenson, Administrator
Jonas Kik, National Dire of Developm

March 7, 1969

The main purpose of the research program at CARIH is to find new methods for the control and prevention of asthma. As part of this program, we are now evaluating a new type of treatment, given by inhalation, for persistent cases of asthma. The drug, disodium cromoglycate, or INTAL, was first introduced in England in 1967 and was found effective and safe. It has now been approved for clinical trials in the USA by the Food and Drug Administration and CARIH is one of the few centers that received a supply of INTAL inhalers.

Naturally, before accepting this offer, we have reviewed all previous reports describing the use of this drug and we are convinced that no undesirable side effects occur. An occasional mild irritation of the bronchial tubes, which is attributed to the inhalation of the powder, is only transient and is easily controlled.

The mechanism by which INTAL works is entirely different from all other drugs used for asthma, and consists mainly in the ability of the drug to inhibit allergic hypersensitivity reactions in the lung. Indeed, there is evidence that the effectiveness of INTAL in many cases reduces or eliminates the need for corticosteroids or for other drugs.

In view of the fact that INTAL is not part of our standard treatment program we thought it advisable to inform you about our new project and to ask for your permission to include your child in our treatment plan. Children who have continued to have asthma despite our treatment efforts here at CARIH, and who require corticosteroids for satisfactory control of their disease, are especially eligible for INTAL treatment, and this is the main reason for recommending your child for this new treatment.

If you would like to discuss this treatment further with us, feel free to write or call us and also discuss this with your doctor if you wish. If you have no further questions, kindly sign below and return this letter promptly so that your child can be included in the ongoing program. Naturally, reports of our findings will be included in our final medical report on your child.

Sincerely yours,

C. J. Falliers, M.D.
Medical Director

CJF:sh

We understand the indications for treatment with INTAL and we agree that our child should participate in the proposed program at CARIH.

children's asthma research institute & hospit
3401 west 19th avenue / denver, colorado 80204 / 433-25
Constantine J. Falliers, M.D., Medical Director
Jack Gershtenson, Administrator
Jonas Kik
National Direc
of Developme

RE: ______________________________

It is our privilege to inform you that, as a reflection of the steadily expanding effort for the understanding and control of intractable asthma, a new research program has developed at CARIH, and we should like to have your (son/daughter), ______________________ participate in it.

As you may know, growth and development, as well as the functions of certain glands, are frequently effected by the steroid drugs, such as cortisone, which are sometimes necessary for severe asthma. We are now able to find out how a child's body reacts to the adminstration of steroids and to their discontinuance (should it prove possible to discontinue this therapy) by means of three basic tests: the first test involves collecting blood and urine specimens during two 48-hour periods to determine certain basic hormone levels under natural conditions. The second test is completed in about 2-1/2 hours and evaluates the response of the body to small amounts of insulin, measuring the elevation of blood and urine hormones in response to a lowering of normal blood sugar. The last test enables us to study the adrenal function during four days before and after the adminstration of a substance called Metopirone. As much as possible the child is ambulatory and normally active during the course of these tests.

Although these tests are now well established medical procedures, we felt it necessary to inform you of our intention to include your child in the study and ask for your authorization because, despite the fact that we have had extensive personal experience with them, they are not part of our usual diagnostic and therapeutic routine for asthma. Also the frequency of the tests, which may be repeated more than once or twice, may lead your child to complain to you and naturally your encouragement and support will be needed to convince him (or her) of the essential nature of these procedures.

We are sure you would also want to know that the tests mentioned have proved to be extremely safe in the hands of many other medical investigators and ourselves as well. The small amounts of insulin given, the constant medical supervision and the fact that even the slightest evidence of excessive drowsiness or neuromuscular irritability is promptly corrected by giving a sugar-containing solution intravenously, serve to indicate that the serious side-effects of insulin administration (temporary loss of consciousness, brief convulsive movements) can certainly be avoided and are not expected to occur. Thus, we believe that the great benefits to be derived for your child, - and for other children as well - far outweigh the discomfort of the test and place your

child under no serious risk whatsoever. The Metopirone test likewise has proved to be safe and the rare symptoms it causes, such as nausea and vomiting, can be promptly eliminated by stopping the test. Whenever medically indicated, additional medication is given to guarantee your child's comfort and safety.

In order to ensure close observation and to guarantee the continuity and reproducibility of these studies, all children participating in these tests live temporarily in a special cottage, similiar in design and construction to the other cottages on our campus. While there, for up to three months they attend regular school on a half-time basis. An experienced tutor is provided the rest of the time to keep interference with the child's school progress at a minimum, and to promote our educational goals.

We should like to believe that the above statements will prove to be sufficient to convince you of the significance and essential nature of the studies described. In addition, you might be interested to know that this program has been approved by the appropriate review committee of CARIH, and has also received the approval and financial support of the National Institute of Child Health and Human Development of the United States Public Health Service. When the study is completed we shall gladly forward all information obtained from these tests to your child's physician at home.

As we should like to have your written permission to proceed as above, we have enclosed two copies of this letter, one for your records and one for you to sign and return to us at your earliest convenience. If you wish to receive further information on our project, in greater detail than could possibly be included in this letter, or if you have any other questions or comments, please feel free to write or call us at (303) 433-2591, extension 46 or 80.

Sincerely yours,

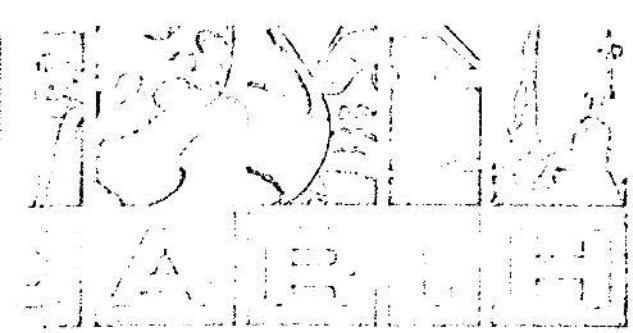
Jacqueline R. Jorgensen, M.D.
Senior Staff Pediatrician

C. J. Falliers, M.D.
Medical Director

JRJ:CJF:sh
Encl.

Date

Date



children's asthma research institute & hospital
3401 west 19th avenue / denver, colorado 80204 / 433-23
Constantine J. Falliers, M.D., Medical Director
Jack Gershtenson, Administrator
Jonas Kilk, National Direct of Develop

RE: _____

Many children at CARIH have received ACTH for the treatment of their asthma and some may need it again in the future. Our staff has given it only rarely because of reports of occasional allergic reactions. Recently, however, a completely synthetic ACTH (Cortrosyn) has been made available to us which is very much less likely to cause such reactions and which we feel will be valuable for treatment of asthma.

Cortrosyn has been tested extensively in other countries and has been found to be safer than ACTH from animal sources. At present Cortrosyn is in the final stage of evaluation before the F.D.A. allows all doctors to prescribe it. Because it offers certain advantages in medical treatment, we would like to give it to some of our children at CARIH. The first step planned is to give single doses to a group of children and measure the changes that occur in the blood for just a few hours. The effects of a single dose of Cortrosyn last less than a day and the child receiving it should notice no effect at all.

Since Cortrosyn has not yet been released to the medical profession for general use, you permission is required before your child may receive it. To indicate your consent, please sign this form below, retaining the copy for your records, and return the original to us as quickly as possible.

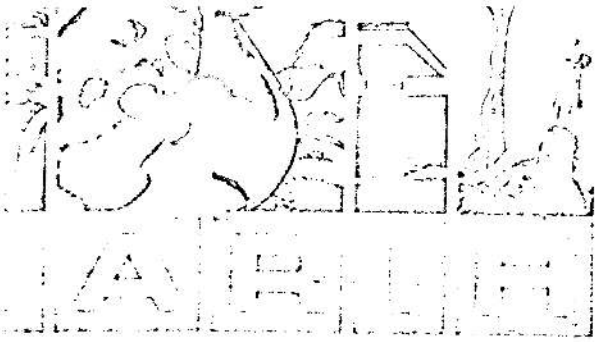
Sincerely yours,

C. J. Falliers, M.D.
Medical Director

CJF:JJ:sh
Encl.

_____
Date

_____
Date



3401 west 19th avenue / denver, colorado 80204 / 433-259
Constantine J. Falliers, M.D., Medical Director
Jack Gershtenson, Administrator
Jonas Kikes, National Director of Development

November 20, 1970

Mr. and Mrs. -----
12345 -----
City, State

RE:

Dear Mr. and Mrs. -----:

As you probably are aware, Rubella (German measles) vaccine has been approved and recommended for general use in the United states for immunization of all susceptable children and since yours son, Richard has no antibodies to Rubella, we would like to immunize him with this vaccine.

We would like to use this opportunity to examine any effects that this may have on the reactivity of the airways and this will be done by checking the response to inhalations of methacholine to your child at intervals over a period of several weeks. This is a routine procedure done at our institute as part of the complete investigation and management of our patients.

This procedure will be carried out under complete supervision and is not harmful in any way. However, we do want you to be informed of this and would appreciate your consent by signing this letter and returning it to us by return mail. The copy is for your file and information.

If there are any questions regarding this, please do not hesitate to contact us.

Sincerely yours,

LM:sh
Encl.

We hereby consent to the Rubella vaccine immunization and study as described above for our child, Richard.

(Father's signature) _____ (Date) _____

(Mother's signature) _____ (Date) _____

children's asthma research institute & hospital
3401 west 19th avenue / denver, colorado 80204 / 433-25
Elliott Middleton, Jr., M.D.,
Director, Clinical Services and Research

PART ONE OF A GENERAL INSTITUTIONAL ASSURANCE

The Children's Asthma Research Institute and Hospital (CARIH) will comply with the policy for the protection of human subjects participating in activities supported directly or indirectly by grants or contracts from the Department of Health, Education and Welfare. In fulfillment of its assurance:

This institution will establish and maintain a committee competent to review projects and activities that involve human subjects. The committee will be assigned responsibility to determine for each activity as planned and conducted that:

The rights and welfare of subjects are adequately protected.

The risks to subjects are outweighed by potential benefits.

The informed consent of subjects will be obtained by methods that are adequate and appropriate.

This institution will provide for committee reviews to be conducted with objectivity and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from reviews of projects or activities in which they have an active role or a conflict of interest.

This institution will encourage continuing constructive communication between the committee and the project directors as a means of safeguarding the rights and welfare of subjects.

This institution will provide for the facilities and professional attention required for subjects who may suffer physical, psychological, or other injury as a result of participation in an activity.

This institution will maintain appropriate and informative records of committee reviews of applications and active projects, of documentation of informed consent, and of other documentation that may pertain to the selection, participation, and protection of subjects and to reviews of circumstances that adversely affect the rights or welfare of individual subjects.

This institution will periodically reassure itself through appropriate administrative overview that the practices and procedures designed for the protection of the rights and welfare of subjects are being effectively applied and are consistent with its assurance as accepted by the Department of Health, Education and Welfare.

Official signing for the Institution: Elliott Middleton

Elliott Middleton, Jr., M. D.
Director, Clin. Svcs & Research
Date: March 17, 1970

EMB